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Automated registration and stitching of multiple 3D ultrasound images for monitoring neonatal intraventricular hemorrhage

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ABSTRACT

Dilatation of the cerebral ventricles is a common condition in preterm neonates with intraventricular hemorrhage (IVH). Post Hemorrhagic Ventricular Dilatation (PHVD) can lead to lifelong neurological impairment caused by ischemic injury due to increased intracranial pressure, and without treatment can lead to death. Previously, we have developed and validated a 3D ultrasound (US) system to monitor the progression of ventricle volumes (VV) in IVH patients; however, many patients with severe PHVD have ventricles so large they cannot be imaged within a single 3D US image. This limits the utility of atlas based segmentation algorithms required to measure VV as parts of the ventricles are in separate 3D US images, and thus, an already challenging segmentation becomes increasingly difficult to solve. Without a more automated segmentation, the clinical utility of 3D US ventricle volumes cannot be fully realized due to the large number of images and patients required to validate the technique in a clinical trials.

Here, we describe the initial results of an automated 'stitching' algorithm used to register and combine multiple 3D US images of the ventricles of patients with PHVD. Our registration results show that we were able to register these images with an average target registration error (TRE) of 4.25±1.95 mm.

Keywords: Neonatal Post Hemorrhagic Ventricular Dilatation, 3D Ultrasound, Image Registration

1. INTRODUCTION

Intraventricular hemorrhage (IVH) is a common condition among preterm infants with an occurrence of 12-20% in babies born at less than 35 weeks.[1] While mild IVH is generally associated with favourable outcome, severe IVH can result in hydrocephalus, which is the abnormal accumulation of cerebral spinal fluid (CSF) within the cerebral ventricles. Children who were born preterm and had hydrocephalus are at increased risk of developmental delays, impaired vision, hearing, and motor skills.

Neonates at risk of IVH are monitored by conventional 2D ultrasound (US) for hemorrhage and potential ventricular dilatation. However, the sensitivity of 2D US to dilatation is poor because it cannot provide accurate measurements of irregular volumes such as the ventricles. Although linear measurements on a single image plane such as the ventricle index or anterior horn width can be performed, they do not reflect the true volumetric change.[2] In addition, treatment differs between hospitals, and the determination of whether to do a surgical intervention is qualitative.[3] Thus, there is the opportunity to improve the quality of patient care by introducing a more quantitative measure to the differential diagnosis.

Previously, our lab has developed and validated a 3D US system to image the cerebral ventricles of neonates with IVH.[4,5] Many patients with severe IVH have ventricles, which dilate rapidly and as such, we have previously imaged dozens of neonates who have ventricles too large to image within a single image volume. This inhibits further automated segmentation development as our previously used method relied on an atlas during part of the segmentation pipeline, and in cases of patients with hydrocephalus, the full ventricle system could be within 2 or more image volumes.[6] In addition to this, the multiple 3D US image volumes are harder to interpret qualitatively from one imaging session to the next by a clinician.

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As such, we describe an initial automated approach to 'stitch' overlapping 3D US images of the neonatal brain together as this could assist in both the further development of segmentation algorithms and to better help clinicians assess patients with highly enlarged ventricles.

The Insight Toolkit (ITK) library[7] in C++ provides a modular image processing framework that can be customized for many purposes. It includes a "registration" class that maintains control of an algorithm for aligning images in multiple dimensions. This registration class requires a "transform" to change the orientation of one image relative to the other by some rule. The registration class also requires a metric to describe how well or poorly a pair of images are aligned in time and space, which the registration seeks to minimize. To prevent the necessity of trying every possible orientation by brute force, the registration class uses one of a number of "optimizers", which seek to make more educated guesses about what next orientation will be better aligned than the current one. These optimizers employ a stopping criteria, based on the step length, difference between metric values, etc. such that when some rule is reached they will exit the process and deliver a result to the registration class. Finally, images are made up of discrete locations, thus an interpolation scheme must be provided to determine where to put the intensity information for a voxel that is located between grid positions after transformation.

2. METHODOLOGY

As part of a larger study, and after an initial diagnosis of IVH, neonatal patients were enrolled with informed parental consent. Images were acquired as per a protocol approved by the local Research Ethics Board.

3D US image acquisition

Images were acquired using a Philips HDI 5000 US machine with a C8-5 transducer. 3D US imaging was performed after placing the ultrasound transducer in a motorized fixture (Fig. 1) that tilted the transducer about the axis at the probe tip through a 35-70° arc[1]. During image acquisition, 2D US images were acquired using a Epiphan VGA2USB LR Solo frame grabber (Epiphan Video, Palo Alto CA) on a laptop computer as the motor tilted the transducer, and in-house software reconstructed the 3D US image in real time as images were received into the computer.[8]

Patients with severe PHVD were imaged in two 3D US image – one of the left lateral ventricle, and one of the right lateral ventricle, both with some mid-line overlap (Fig. 2 – ultrasound images of left and right ventricles). Images were taken on the same day within 2-5 minutes of each other.

Automated registration pipeline

To facilitate aligning multiple overlapping 3D US images, an image registration pipeline was developed using the Insight Toolkit (ITK) library [7] in C++. The generic image registration class in ITK applies a transform to one image in each iteration (moving image), and then calculates a cost function based on image intensity to determine how well aligned it is to the other image (fixed image). To avoid brute force iterating over every possible orientation, the transform is altered in each iteration according to an optimization protocol. We initialized with a Powell method optimizer, chosen for its computational efficiency as it does not require the calculation of derivatives[9]. While Mattes Mutual Information (MMI) was chosen in a previous study as a cost function metric[10], the pipeline required initialization using fiducials, and required user input, which could introduce error. We implemented Normalized Cross Correlation (NCC) as our cost function as it requires no such user-initialization and performs better when large rotations are required[11]. A rigid 3D versor transform was used as it was assumed no deformation would occur over the short time between 3D image acquisitions, and this was supplied to the image registration pipeline. The versor transform was chosen over a Euclidian transform for the stability of optimization due to smooth rotational trajectories[12]. To facilitate fast computation, the images were subsampled by a factor of 8, reducing processing time substantially. A common point of rotation was chosen corresponding to the location of the probe tip, where the images were known to intersect. The resulting registered moving-image was blended pixel-by-pixel with the fixed-image by using a simple averaging filter with the fixed-image data according to Equation 1:

$$f(x,y,z) = \begin{cases} a_{i,j,k} \text{ if } b_{i,j,k} = 0 \\ b_{i,j,k} \text{ if } a_{i,j,k} = 0 \\ \frac{a_{i,j,k}+b_{i,j,k}}{2} \text{ otherwise} \end{cases} \quad (1)$$

Where $a_{i,j,k}$ and $b_{i,j,k}$ pixel intensities of the fixed and transformed moving image at coordinates (x,y,z).

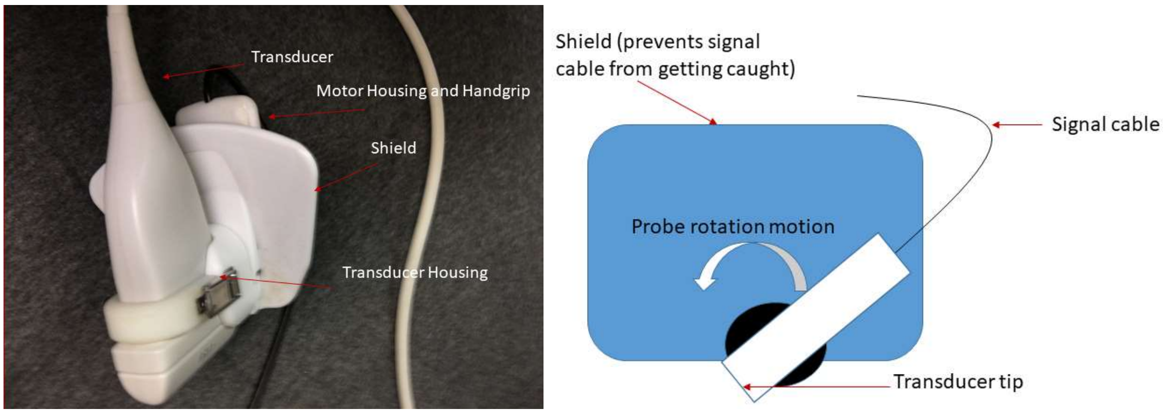

Figure 1 – left: The handheld motorized transducer housing with transducer attached, right: schematic of tilt scanner operation."Shield" region protects user from making contact with the moving transducer, keeps cable from becoming tangled, and indicates where the probe will be at maximum scan angle.

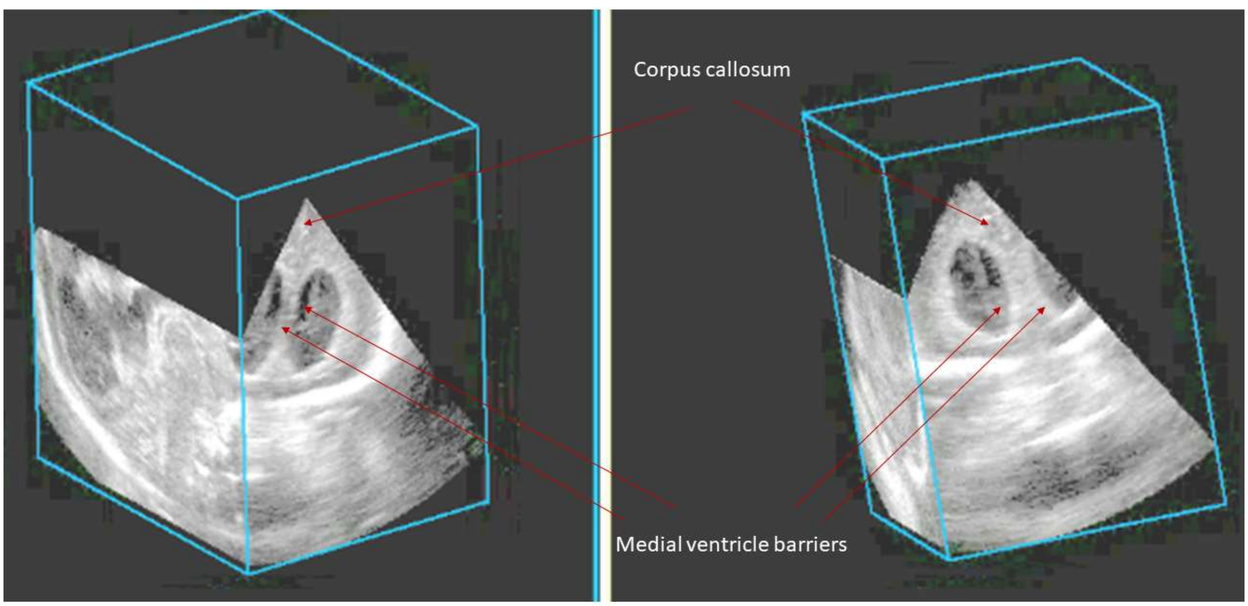

Figure 2 – A patient with PHVD showing the a) left and b) right lateral ventricle images. Midline structures such as the corpus callosum and medial ventricle barriers show overlap in both images with partial overlap of some of the ipsilateral ventricle on the 'right' or 'left' image.

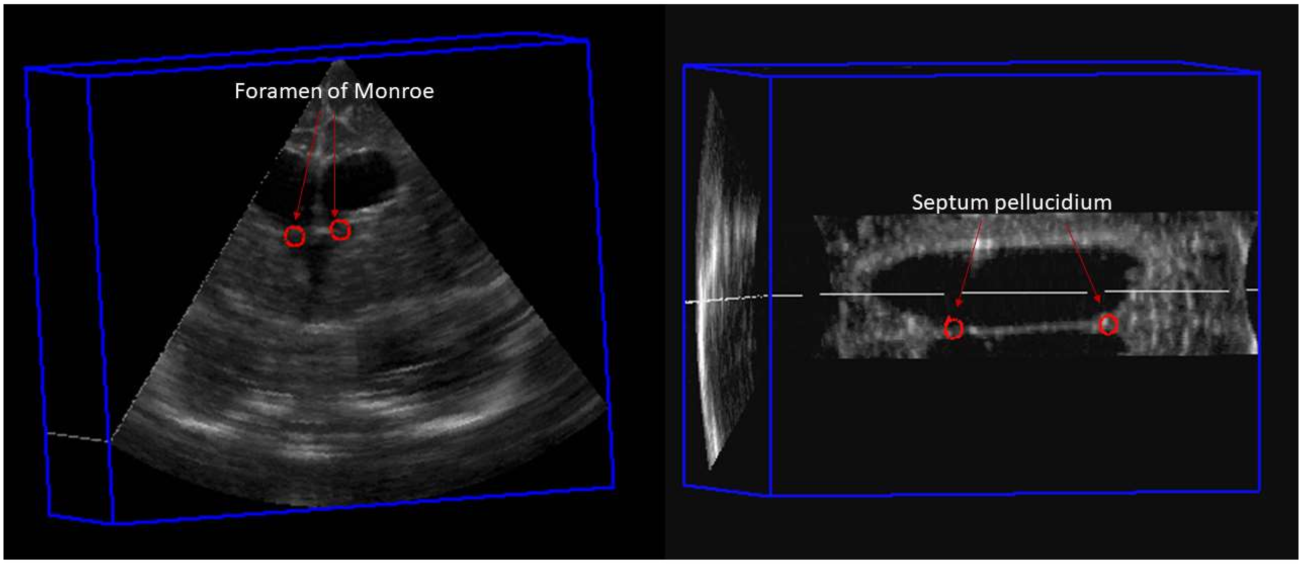

Figure 3 – 3DUS images showing a coronal view with the right and left foramen of Monro highlighted, transverse view with the anterior and posterior limit of the septum pellucidium highlighted

Prior to validating the registration it was necessary to evaluate whether the trained user responsible for selecting anatomical landmarks was able to select these consistently. To validate the trained user's consistency in selecting anatomical landmarks, the average Fiducial Localization Error (FLE) was determined using one image, with the user selecting the same four anatomical landmarks on subsequent days. One anatomical landmark that was sought in each image was the foramen of Monroe between each lateral ventricle and the third ventricle. Another was the septum pellucidi between the lateral ventricles (Fig. 3). Euclidian distance was used to evaluate how consistently the user identified the same structures.

The registration was validated by selecting homologous anatomical landmarks (foramen of Monroe and septum pellucidi) in both the fixed-image and transformed moving-image, and an average Target Registration Error (TRE) was calculated based on Euclidian distance between the corresponding test points selected by the user. These structures were chosen because they occur close to the midline between the cerebral hemispheres, which was the region of partial overlap between the images. Average TRE was calculated based on selection of four landmarks by the trained user previously validated on 7 registered images, with fiducials selected in the fixed and moving images 48 hours apart and in separate files to prevent user bias.

Manual landmark registration

The clinical utility of the automated registration pipeline is dependent on requiring less time and effort than the equivalent practice without automation. To validate this, a landmark registration was performed on each pair of images that were successfully automatically registered using alternate homologous features to those being used for validation. The manual registration was performed by importing the fixed- and moving-image into 3D Slicer (https://www.slicer.org/)[13], and using the built-in landmark registration tool. The TRE for the landmark registration was calculated using the same features used to calculate the automated registration TRE.

3. RESULTS

The average FLE was calculated based on a trained user repeatedly selecting points indicating the two foramen of Munro and the anterior and posterior limits of the septum pellucidi in a single image. The fiducials were selected at a minimum of 24-hour intervals over the course of several days to allow a wash-out period such that the user couldn't simply select identical points a few minutes apart. The mean FLE of the positions selected as fiducials was 2.8 mm.

Nine patients with severe PHVD were used in this study. Two of the image registrations were considered failures based on qualitative observation of the result and omitted from TRE calculation. The TRE for 9 image registrations was measured based on anatomical landmarks selected from the fixed and moving images. The fiducial markers were selected in the fixed and moving images two days apart, to prevent selection bias by the trained user. The average and standard deviation of the TRE were calculated for the group of 7 images where registration was a qualitative success, and found to be 4.25±1.95 mm. This is compared with the mean TRE for a manual registration of 8.39±4.78 mm. An example case of successful automatically registered and stitched images are shown in Figure 4.

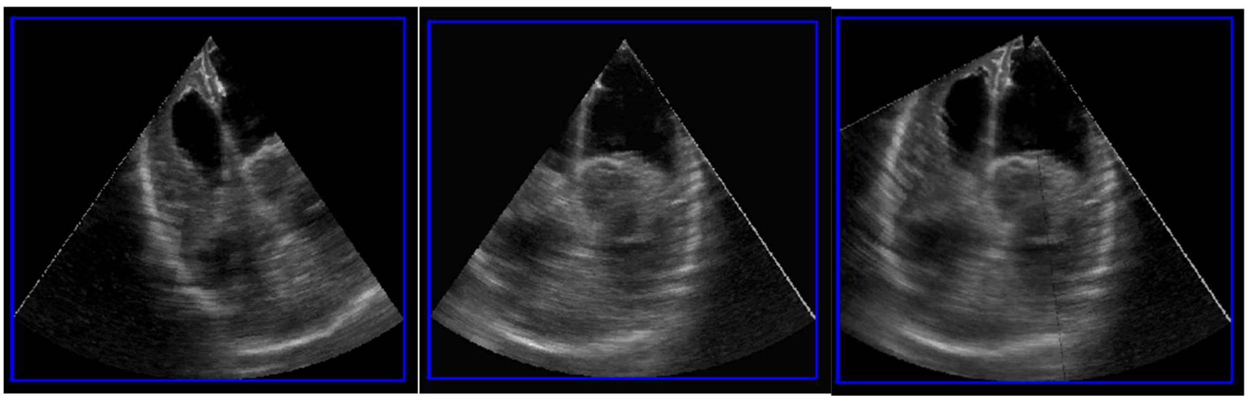

Figure 4 – Example of successful registration and stitching: left and right component images on the left, and stitched image on the right.

The mean registration time for the automated algorithm was 38.6±10.8 seconds, measured for the 7 successful registrations using a desktop computer running Windows 10 (Microsoft, Redmond WA) with an Intel Core(TM) i7-5820K CPU @ 3.30GHz, 3301 MHz, processor, with 6 Cores, 12 Logical Processors (Intel, Santa Clara CA) and 64 GB RAM. This compares with a mean of 299.9±70.0 seconds when a landmark registration was performed on the same set of images using 3D Slicer (including time for selection of the landmarks).

The registration pipeline suffered a failure in two of the nine cases included in the study, with an example of a failed registration shown in Figure 5.

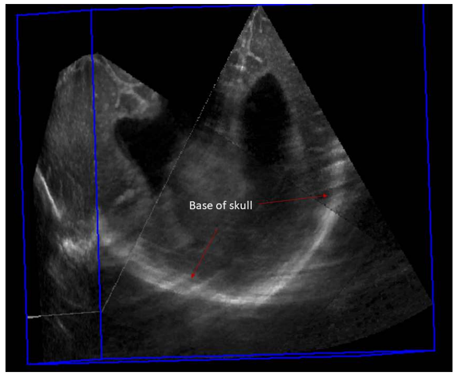

Figure 5 – Example of a failed registration. Note the continuous line formed by the back of the skull even though the anatomy does not match up.

4. DISCUSSION

An automated image registration and stitching pipeline for neonatal 3DUS has been validated with 77% success rate and an average TRE of 4.25 ±1.95 mm, with a processing time of 38.6±10.8 seconds. This TRE is based on the trained user in the study validating ability to select anatomical landmarks with a FLE of 2.8 mm. This was an improvement over the manual registration TRE of 8.39±4.78 mm with a mean time of 299.9±70.0.

Although the cost metric appeared to be optimized in the failure cases, a human user can tell the internal structures are not aligned (i.e. ventricles, brain matter). This is indicative of a local minimum in the cost function that the optimizer has settled in. This could be caused by the somewhat symmetrical nature of the skull. One possible solution for this could be performing the registration using all image data to get the skull aligned, then filtering out high intensity features (i.e. the bones of the skull) and performing the registration on brain matter only.

The results of this study open the door to a more quantitative, standardized method of determining which patients need a surgical intervention, as well as when. Future work will examine potential fixes to failed image stitching, and using an atlas based segmentation approach on these images with comparison to time matched MRIs.

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